REMARKS

I. Detailed Action

A. Election/Restrictions

The Examiner acknowledges Applicants' election with traverse of Group I, claims 1-8 and 12-19 and SEQ ID NO: 35. Applicants acknowledge that claims 9-11, 20-22 and claims drawn to SEQ ID NO:37, 39, 41, 43 and 45 are withdrawn from consideration as being drawn to a non-elected invention.

B. Sequence Listing

The Examiner acknowledges Applicants' CRF and paper sequence listing as being entered.

C. Priority

The Examiner notes the status of parent application No. 09/352,168 and 09/352,159 should be updated. Applicants have now amended the specification and application data sheet to indicate that the above two applications have issued as U.S. Patent Nos. 6,211,434 and 6,211,435, respectively.

D. Specification

The Examiner states the disclosure is objected to because of the following informalities:

Page 59, line 15 cites sequence without a sequence identifier, and page 68, line 25, cites a hyperlink directed to an Internet address. Applicants have now amended page 59, line 15 to include a reference to SEQ ID NO:54. In addition, Applicants are also submitting a new CRF and paper copy of the sequence listing, including the sequence on page 59. In addition, Applicants have now amended the specification on page 68, to remove the hyperlink and instead just recite the Internet address. Applicants thank the Examiner for pointing out these errors.

E. Claim Objections

The Examiner states claims 1-8 and 12-19 are objected to for reciting non-elected inventions. All claims have been limited to the elected sequence of SEQ ID NO: 35.

II. Claim Rejections - 35 U.S.C. § 112, Second Paragraph

Claims 1 and 12-19 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The Examiner rejects claim 1 as indefinite for failing to recite proper Markush terminology. The Examiner suggests that --the group consisting of-- be inserted after "from". Applicants have now amended claim 1 in the manner suggested by the Examiner, thereby alleviating this rejection. Applicants also noted that originally filed claim 12 required the same amendment in order to recite proper Markush terminology. The Examiner's suggested amendment has therefore also been made to correct claim 12.

Claims 12-19 stand rejected as indefinite for failing to recite the specific hybridization and wash conditions required for the claimed "high stringency" conditions. In addition the Examiner suggests that --sequence--, should be inserted before "identity" to clarify that the identity is assessed based on sequence. Applicants have now amended each of the claims to recite "sequence" before identity and to include the exemplary high stringency conditions as given on page 15 of the specification as originally filed. No new matter has been added.

In light of the above amendments and remarks, Applicants assert claims 1 and 12-19 are now in a condition for allowance. Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, second paragraph.

III. Claim Rejections - 35 U.S.C. § 112, First Paragraph

A. Enablement

Claims 1-8 and 12-19 stand rejected by the Examiner under 35 U.S.C. § 112, first paragraph because the specification, while being enabling for an isolated polynucleotide of SEQ ID NO: 35 encoding the fumonisin degrading enzyme of APAO, transgenic plant/plant cell/seed comprising said polynucleotide, does not reasonably provide enablement for any polynucleotide comprising at least 20 contiguous bases of SEQ ID NO: 35, a polynucleotide comprising at least 70%, 80%, and 90% sequence identity to SEQ ID NO: 35 or a polynucleotide that hybridizes thereto under high stringency conditions, complementary polynucleotides, and transformed plants/plant cells/seed comprising said polynucleotide.

Applicants respectfully traverse this rejection. Amended independent claims 1-4, 7-8, 12-15, 18, and 19 now include the functional limitation that the claimed polynucleotide sequences encode a protein having fumonisin degrading activity. Further, these claims have been amended to require sequences that share at least 90% or 95% sequence identity to SEQ ID NO: 35. Applicants have also amended all independent claims to recite polynucleotides with at least 200 contiguous bases of SEQ ID NO: 35. Applicants assert that the amended claims are enabled by the originally filed specification.

To be enabling under 35 U.S.C. §112, a patent must contain a description that enables one skilled in the art to make and use the claimed invention. Applicants have provided the novel polynucleotide sequence of SEQ ID NO: 35 and its encoded protein set forth in SEQ ID: 36. The variant sequences being claimed represent those having at least 90% or 95% sequence identity to SEQ ID NO: 35 and which encode a protein having fumonisin degrading activity, and those sequences that additionally hybridize to the full length complement of SEQ ID NO: 35 under stringent conditions, which also encode a protein having fumonisin degrading activity. Therefore, the claimed sequences of the invention vary from the novel disclosed sequence by well-defined structural parameters (i.e., percent sequence identity to SEQ ID NO: 35). Applicants have provided sufficient guidance for how to make or isolate variant sequences having the structural and functional limitations recited in these claims.

The Examiner states that obtaining polynucleotides having the structural and functional characteristics as set forth in the claims would require extensive and undue experimentation. Applicants respectfully disagree. Applicants cite *In re Wands*, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988) as providing guidance to determine how the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art. When determining the quantity of experimentation necessary, the focus is not on the amount of experimentation necessary to practice the entire genus, but rather the amount of experimentation required to practice any particular member. This concept is central to the holding in *In re Wands,* where the claims read on the use of any IgM antibody that possessed a particular binding affinity. Clearly, the court recognized that it would require an infinite amount of experimentation to obtain every single possible IgM antibody that could be generated

with the specified affinity. Accordingly, the court focused on the amount of experimentation necessary to practice any particular IgM antibody with the recited binding affinity, and not the amount of experimentation required to practice the entire genus. This focus is further exemplified by the multitude of chemical patents that have issued that contain generic claims reading on tens to hundreds of thousands of individual members.

The question then becomes how much experimentation is required to isolate or construct the claimed polynucleotide sequences. Applicants submit that no more than routine experimentation is required. This may be accomplished by a variety of methods such as routine screening of DNA libraries for the hybridization to the recited sequences so as to identify positive clones, amplifying the nucleic acids of interest from nucleic acid samples, and even preparation of nucleic acids of interest by direct chemical synthesis (see for example the sections entitled "Nucleic Acids", "Construction of Nucleic Acids" and "Synthetic Methods for Constructing Nucleic Acids" on pages 23-25 of the originally filed specification). Nucleotide sequences having homology to the recited sequences may also be obtained by mutagenesis or a variety of recombinant methods known to those skilled in the art. Accordingly, no more than routine experimentation is required to identify sequences which are 90% or 95% identical to the recited sequences or other polynucleotides that encode polypeptides with fumonisin degrading activity.

Given this disclosure, one of skill in the art could readily take the novel nucleotide sequence of SEQ ID NO: 35, obtain a sequence having at least 90% or 95% sequence identity to SEQ ID NO: 35 either by modifying this coding sequence or by isolating such variant sequences, test for the fumonisin degrading activity of the encoded polypeptide, and subsequently clone the variant nucleotide sequence into an expression cassette, transform plant cells, and regenerate plants comprising fumonisin degrading proteins without undue experimentation. In this regard, Applicants note that the Federal Circuit has repeatedly stated that enablement is not precluded by the necessity for some experimentation, so long as the experimentation needed to practice the invention is not undue. *In re Wands,* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). Furthermore, a considerable amount of experimentation is permissible, if it is merely *routine*, or

if the specification provides a reasonable amount of guidance in which the experimentation should proceed. *Id.*

In support of the rejection of the claims as not being enabled by the specification, the Office Action raises the issue of unpredictability of the claimed invention in view of two references in the art. The Examiner cites that the state of the art teaches that structural identity between two DNA/protein sequences does not necessarily mean that the sequences have the same function. The Examiner cites Lazar *et al.* (MCB 1988 8(3):1247-1257) and Broun *et al.* (Science 1998 282:131-133) which each provide examples of very specific limited amino acid changes which resulted in elimination or alteration of the experimental protein's catalytic activity. Applicant notes that Lazar *et al.* state "When aspartic acid 47 was mutated to alanine or asparagine, biological activity was retained..." (page 1247, Abstract), so Lazar *et al.* demonstrate that not all substitutions, including non-conservative ones as noted above, impact the biological activity of a protein. Broun *et al.* actually note the high sequence similarity between the oleate 12-desaturase and oleate hydroxylase and use this to identify seven residues conserved in desaturases and to target them for modification and activity (see page 131, column 2 – column 3). Broun *et al.* actually use the sequence similarity of the desaturase and the hydroxylase to predict which residues to change to alter the activity of the desaturase. Similarly, the disclosure of SEQ ID NOS: 35-45, their similarity to other known APAO sequences (for example, the working examples given on pages 58-61 and page 68), the guidance on sequence analyses, comparison, and identity (for example, page 17-21), the guidance on codon degeneracy, silent variants, and preferences (pages 9-10), the guidance on conservative amino acid substitutions (pages 9-10), and the ready availability in the art for assays for fumonisin degrading activity (see working examples 1 and 5) show that the specification coupled with the knowledge in the art enables a person in the art to make and use sequences having 90% or 95% sequence identity to SEQ ID NO: 35 having fumonisin degrading activity.

The Examiner also cites *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at 1027 (Fed. Cir. 1991). At page 1027 it is taught that the disclosure of a few sequences did not enable claims broadly drawn to any analog thereof.

In *Amgen v. Chugai*, the Federal Circuit concluded that the patent specification was insufficient to enable one of ordinary skill in the art to make and use the invention claimed in claim 7 of the '008 patent without undue experimentation. As stated on page 1027, however, "it is not necessary that a patent applicant test all the embodiments of his invention, citing *In re Angstadt*, 537 F.2d 498, 502, 190 USPQ 214, 218 (CCPA 1976); what is necessary is that he provide a disclosure sufficient to enable one skilled in the art to carry out the invention commensurate with the scope of his claims. For DNA sequences, that means disclosing how to make and use enough sequences to justify grant of the claims sought." Applicants respectfully submit, that has been done in the instant specification. The present invention discloses how to make and use the sequences of the invention, as discussed in the paragraph above.

In view of these amendments and remarks, Applicants respectfully submit that the specification is enabling for the pending claims. Therefore, Applicants respectfully request that the rejection of claims 1-8 and 12-19 under 35 U.S.C. 112, first paragraph, for lack of enablement, be withdrawn.

B. Written Description

Claims 1-8 and 12-19 stand rejected by the Examiner under 35 U.S.C. § 112, first paragraph as containing subject matter which is not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Examiner states the claims do not recite functional language and the specification only describes the unmodified polynucleotides of the *Exophiala spinifera* isolates from maize and that substantial variation in structures and function are expected among polynucleotides that share 20 contiguous bases. The Examiner states that the disclosure of SEQ ID NO: 35 does not provide adequate written description for all the nucleotides having at least 70%, 80%, and 90% sequence identity to SEQ ID NO: 35, all polynucleotides that hybridize thereto under high stringency conditions, and all polynucleotides comprising at least 20 contiguous bases of SEQ ID NO: 35, having no known function.

Applicants respectfully traverse this rejection. Applicants have amended the claims to recite they must encode a protein with fumonisin degrading activity. Furthermore, the claims have been amended to require sequences that share at least 90% or 95% sequence identity to SEQ ID NO: 35. Applicants have also amended all independent claims to recite polynucleotides with at least 200 contiguous bases of SEQ ID NO: 35. Applicants assert that the amended claims are enabled by the originally filed specification.

The recitation of at least 90% or 95% nucleotide sequence identity is a very predictable structure of the sequences encompassed by the claimed invention. The Examiner is reminded that the description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. 66 Fed. Reg. 1099, 1106 (2000). Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the Applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. 66 Fed. Reg. 1099, 1106 (2000). Applicants submit that the knowledge and level of skill in the art would allow a person of ordinary skill to envision the claimed invention, i.e., a sequence having at least 90% or 95% sequence identity to the sequence set forth in SEQ ID NO: 35.

Furthermore, the description of a claimed genus can be by structure, formula, chemical name, or physical properties. *See Ex parte Maizel*, 27 USPQ2d 1662, 1669 (B.P.A.I. 1992), *citing Amgen v. Chugai*, 927 F.2d 1200, 1206 (Fed. Cir. 1991). A genus of DNAs may therefore be described by means of a recitation of a representative number of DNAs, defined by nucleotide sequence, falling within the scope of the genus, *or* by means of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1569 (Fed. Cir. 1997); *see also* Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, first paragraph, "Written Description" Requirement, 66 Fed. Reg. 1099, 1106 (2000). The recitation of a predictable structure of at least 90% or 95% sequence identity to SEQ ID NO: 35 is sufficient to satisfy the written description requirement.

An Applicant, however, may also rely upon functional characteristics in the description, provided there is a correlation between the function and structure of the claimed invention. *Id., citing Lilly* at 1568. To expedite prosecution, the claims have been amended to further recite functional characteristics of the claimed genus. Specifically, the amended independent claims require that sequences sharing at least 90% or 95% sequence identity to SEQ ID NO: 35 encode a protein having fumonisin degrading activity; thereby providing a functional characterization of the sequences claimed in the genus.

Example 14 of the Revised Interim Written Description Guidelines is directed to a generic claim: a protein having at least 95% sequence identity to the sequence of SEQ ID NO:3, wherein the sequence catalyzes the reaction A → B. The Training Materials concludes that the generic claim of Example 14 is sufficiently described under § 112, first paragraph, because 1) "the single sequence disclosed in SEQ ID NO:3 is representative of the genus" and 2) the claim recites a limitation requiring the compound to catalyze the reaction from A → B. The Guidelines conclude that one of skill in art would recognize that the Applicants were in possession of the necessary common attributes possessed by the members of the genus.

Following the analysis of Example 14, Applicants submit that the amended claims satisfy the written description requirements of § 112, first paragraph. Specifically, the claims of the present invention encompass sequences having at least 90% or 95% sequence identity to the sequence of SEQ ID NO: 35, wherein the claimed sequence encodes a protein having fumonisin degrading activity. As in Example 14, the specification discloses the nucleic acid sequence of SEQ ID NO: 35, and the amended claims recite a limitation requiring the compound to have a specific function (i.e., fumonisin degrading activity).

Consequently, contrary to the Examiner's conclusion, the sequences encompassed by the genus of sequences recited in the amended claims 1-8 and 12-19 are defined by relevant identifying physical and chemical properties. In fact, the common attributes or features of the elements possessed by the members of this genus of sequences is that they encode proteins having fumonisin degrading activity and share at least 90% or 95% sequence identity at the nucleotide level to the disclosed nucleotide sequence of SEQ ID NO: 35. The necessary common features of the claimed genus are clear.

In summary, the description of a representative number of species *does not* require the description to be of such specificity that it would provide individual support for each species that the genus embraces. Applicants submit that the relevant identifying physical and chemical properties of the disclosed genus of the amended claims would be clearly recognized by one of skill in the art and consequently, Applicants were in possession of the necessary common attributes or features of the elements possessed by the members of the genus.

In light of the above amendments and remarks, Applicants respectfully request reconsideration and withdrawal of the rejections to claims 1-8 and 12-19 under 35 U.S.C. § 112, first paragraph, for lack of written description.

IV. Double Patenting

Claims 1-8 and 12-19 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6,211,434. The Examiner states that although the conflicting claims are not identical, they are not patentably distinct from each other because the invention claimed in both the application and the issued patent encompasses SEQ ID NO: 35 and transgenic plants, plant cells and seed comprising SEQ ID NO: 35. The Examiner states the two inventions relate as to species-genus.

Applicants are herein submitting a Terminal Disclaimer in compliance with 37 C.F.R. § 1.321(c), which disclaims any term of a patent issuing from this application which would extend beyond the term of U.S. Patent No. 6,211,434. Therefore, Applicants submit that the claims are in proper form for allowance and respectfully request reconsideration and withdrawal of the obviousness-type double patenting rejection.

V. Claim Rejections - 35 U.S.C. § 102

Claims 12-19 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Duvick *et al.* (U.S. Patent No. 5,792,931, the '931 patent). The Examiner states that Duvick *et al.* teaches an isolated nucleic acid sequence, from *Exophiala spinifera,* encoding a polypeptide having fumonisin detoxification activity, expression vector, and transformed plant, plant cells and seed expressing said nucleic acid (columns 20, 24-30 and 39-40). The Examiner further states the

isolated nucleic acid sequence disclosed by Duvick would inherently hybridize to SEQ ID NO: 35 under high stringency conditions, since "high stringency conditions" is open to individual interpretation.

Applicants respectfully traverse. Applicants have defined high stringency as described earlier. For a rejection under 35 U.S.C. § 102 to be proper, each and every element of the claimed invention must be present in the claim. Claim 1 requires the use of SEQ ID NO: 35 as a reference sequence. The '931 patent does not teach, disclose or suggest SEQ ID NO: 35. Thus, the '931 patent cannot possibly be enabling for a sequence hybridizing to SEQ ID NO: 35. Without SEQ ID NO: 35 one could not know what other sequence would be encompassed by the claims which recite SEQ ID NO: 35. Further, Applicant submits that this rejection is really under 35 U.S.C. § 102(e) as the issue date of the patent and thus its availability as a printed publication under § 102(b) is less than one year before our filing date. The '931 patent does not anticipate the present invention under §102(e) for the reasons described above.

In light of the above, Applicants respectfully request the Examiner withdraw the rejection of claims 12-19 under 35 U.S.C. § 102(b) as anticipated by Duvick *et al.* (U.S. Patent No. 5,792,931).

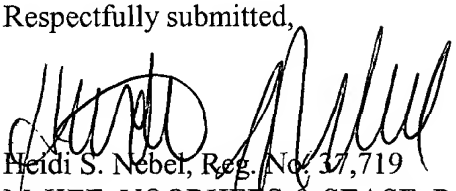
VI. Conclusion

In conclusion, Applicants submit in light of the above amendments and remarks, the claims as amended are in a condition for allowance, and reconsideration is respectfully requested.

This is a request under the provision of 37 C.F.R. § 1.136(a) to extend the period for filing a response in the above-identified application for one month from April 13, 2003 to May 13, 2003. Applicant is a large entity; therefore, please charge Deposit Account No. 26-0084 for the amount of $110.00 to cover the cost of the extension. No other fees or extensions of time are believed to be due in connection with this amendment; however, consider this a request for any extension inadvertently omitted, and charge any additional fees to Deposit Account No. 26-0084.

Reconsideration and allowance is respectfully requested.

Respectfully submitted,



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